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Intellectual Property
ALTANA Pharma AG

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing

(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION

See paragraph 2 below

International application No.
PCT/EP2004/053544

International filing date (day/month/year)
16.12.2004

Priority date (day/month/year)
16.12.2003

International Patent Classification (IPC) or both national classification and IPC
C07D471/04, A61K31/4184

Applicant
ALTANA PHARMA AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for International preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
Fax: +49 89 2399 - 4465

Authorized Officer

Deutsch, W

Telephone No. +49 89 2399-8281



Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and Industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
- ☒ claims Nos. 10 with respect to industrial applicability

because:

- ☒ the said international application, or the said claims Nos. 10 relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the whole application or for said claims Nos.
- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
 - the written form ☐ has not been furnished
 - ☐ does not comply with the standard
 - the computer readable form ☐ has not been furnished
 - ☐ does not comply with the standard
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	1-10
	No: Claims	
Inventive step (IS)	Yes: Claims	1-10
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-9
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

III.

For the assessment of the present claim 10 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Claim 10 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

V.

1 Reference is made to the following documents:

- D1 : WO 97/47603 A (ASTRA AKTIEBOLAG; AMIN, KOSRAT; DAHLSTROEM, MIKAEL; NORDBERG, PETER; S) 18 December 1997 (1997-12-18)
- D2 : WO 02/34749 A (BYK GULDEN LOMBERG CHEMISCHE FABRIK GMBH; BUHR, WILM; KOHL, BERNHARD;) 2 May 2002 (2002-05-02)
- D3 : WO 01/72756 A (BYK GULDEN LOMBERG CHEMISCHE FABRIK GMBH; SENN-BILFINGER, JOERG; BUHR,) 4 October 2001 (2001-10-04)
- D4 : WO 00/63211 A (BYK GULDEN LOMBERG CHEMISCHE FABRIK GMBH; SENN-BILFINGER, JOERG) 26 October 2000 (2000-10-26)
- D5 : WO 98/42707 A (BYK GULDEN LOMBERG CHEMISCHE FABRIK GMBH; SENN-BILFINGER, JOERG; GRUND) 1 October 1998 (1998-10-01)
- D6: KAMINSKI J J ET AL: "ANTIULCER AGENTS. 5. INHIBITION OF GASTRIC H⁺/K⁺-ATPASE BY SUBSTITUTED IMIDAZOL1,2-A PYRIDINES AND RELATED ANALOGUES AND ITS IMPLICATION IN MODELING THE HIGH AFFINITY POTASSIUM ION BINDING SITE OF THE GASTRIC PROTON PUMP ENZYME" JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, vol. 34, 1991, pages 533-541, XP000919185 ISSN: 0022-2623

D7: KAMINSKI J J ET AL: "ANTIULCER AGENTS CONFORMATIONAL CONSIDERATIONS AND THE ANTIULCER ACTIVITY OF SUBSTITUTED IMIDAZO 1,2-a PYRIDINES AND RELATED ANALOGUES" January 1989 (1989-01), JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, PAGE(S) 1686-1700 , XP002008622 ISSN: 0022-2623

Novelty

The compounds of the present claims differ from those of D1, through the fact that they relate to tricyclic compounds rather than the bicyclic benzimidazoles of D1.

The compounds of the present application differ from those of D2-D7 through the fact that they contain a benzimidazole moiety rather than an imidazo[1,2-a]pyridines.

Inventive Step

The closest prior art is considered to be D2 to D5, in view of the fact that these disclose compounds, which are structurally very similar to those of claim 1 and which have the same use in the inhibition of gastric excretion and exhibit gastric and intestinal protection.

The difference between the compounds of the present application and those disclosed in D2 to D5 lies in the position of the nitrogen in the fused 5-membered ring.

In view of the fact that the exchange of carbon and nitrogen is common in the pharmaceutical field and that structurally related benzimidazole compounds are known from D1 to be suitable for the prevention and treatment of gastrointestinal inflammatory diseases, the skilled person would expect that the claimed compounds would retain the desired activity.

The problem underlying the present invention must therefore be the provision of further compounds with unexpected properties compared with the closest prior art. In the absence

of any evidence for these unexpected properties, an inventive step cannot at present be acknowledged for claim 1 and dependent claims.

The compounds of claim 7 are intermediates in the preparation of the final products. These make a structural contribution to the differentiating features of the final compounds. An inventivestep can only be be acknowledged for these compounds if it is shown that the endproducts are inventive.

VII.

Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the documents D1-D5 is not mentioned in the description, nor are these documents identified therein.